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AN UNUSUAL METHOD OF PERFORMING HYSTEROMYOMECTOMY.

By Otto G. Ramsay, M. D., *Instructor in Gynecology, Johns Hopkins University, Baltimore, Md.*

An article in the Johns Hopkins Hospital Bulletin of March, 1900, by Dr. Kelly, entitled "A Preliminary Report on the Surgical Treatment of Complicated Fibroid Tumors of the Womb, with a Description of Two New Methods," describes two unusual methods of performing hysteromyomectomy in difficult cases, which reminds me of a somewhat similar operation I performed for the removal of a myomatous uterus on September 23rd, 1898.

The patient, admitted to The Johns Hopkins Hospital complaining of "tumors of the womb," was 29 years of age, and had been sick for about seven years, beginning at that time to complain of abdominal pains. The abdominal tumor was first noticed by her six years ago, and it had increased in size considerably since then.

On examination, the abdomen was found distended, especially in its lower portion, by a symmetrical tumor, which, on palpation, was found to be composed of several nodules, the largest measuring about 15 by 15 cm.

By vaginal examination, a rounded tumor was felt lying in the cul-de-sac behind the cervix and extending downward between the rectum and the vagina nearly to the vaginal outlet. The cervix could not be found by the vagina, even under ether, being displaced above the symphysis, and the tumor itself was lying quite firmly pressed against the symphysis, giving the impression that the tumor was adherent in the cul-de-sac. This rounded tumor was connected directly with the masses felt through the abdominal wall, and on pressure through the vagina the abdominal mass could be moved slightly. It was, however, impossible to move the growth much by making pressure either through the vagina or through the rectum. (See Fig. 1.)

Operation.—The usual median incision was made, taking the precaution to enter the peritoneal cavity high up rather than in the usual position, so as to avoid an elevated bladder. (Kelly.) On entering the peritoneal cavity, the bladder was found displaced upward, and when the incision was lengthened, it was seen bulging out above the symphysis pubis. On examining the relations of the tumor-mass and the surrounding structures to decide in what manner it might be best attacked, it was found that it could not be delivered through the incision usually made in a hysteromyomectomy, and, on further examination, the reason for this was discovered to be the extension of the growth into the cul-de-sac.

As the usual transverse operation could not be made, the next question was, by what new plan the growth might be removed. The tubes, with the broad ligaments and ovaries, were found raised up but lying somewhat anterior to the main mass of tumor, and on tracing them to their origin, the tumor was found to have arisen entirely from the fundus and posterior surface of the uterus, and the cervix and lower por-

tion of the body of the uterus could be recognized lying covered by the bladder on the anterior surface of the tumor proper. (See Fig. 2.)

In the first place, the vesical peritoneal reflection onto the uterus, which was much higher than usual, was definitely recognized and the peritoneum at this point incised, the bladder was then pushed down for a distance of 5 or 6 cm., exposing the lower portion of the body of the uterus and the cervix. When this had been accomplished, the uterine vessels on each side could be felt pulsating distinctly where they passed to the cervix. The plan of the operation which I then determined to follow was to tie the uterine vessels on both sides, then to cut across the cervix, and after that, to deliver the tumor from the cul-de-sac, thus reversing the usual steps in the operation. I first freed the ovaries from the tumor by a series of ligatures near the uterine cornu, as it was my intention not to remove them; this was easily accomplished, as their relations were not much distorted from the normal. The uterine arteries were tied just at the point where they curve up to reach the cervix. Then, as previously determined, the uterus was cut across from side to side, thus loosening the tumor entirely from its cervical and broad ligament attachments. The tumor was then fixed in the abdominal cavity only by its extension into the cul-de-sac; on attempting to raise it from this position, it was found densely adherent to the whole cul-de-sac and to the rectum posteriorly. These adhesions were carefully separated by raising the tumor slowly and dividing them with the finger as they came into view. The densest adhesions were found between the rectum and the tumor, and here some difficulty was experienced in the detachment, though a slow removal prevented any injury to the rectal coats. After removal of the tumor the remainder of the operation was carried out in the usual manner, the amputated cervix was closed in with catgut sutures, and the bare area on the floor of the pelvis covered by drawing the anterior and the posterior layers of the peritoneum together with catgut sutures. The large overdistended bladder was left puckered over the cervix, and the wound appeared as usual after a normal hysteromyomectomy. Several oozing points on the rectum were checked by fine catgut sutures, the peritoneal cavity was cleansed and the abdominal incision closed in the usual manner.

The convalescence was normal, save for a slight collection of blood above the stump of the cervix between it and the bladder, which was easily evacuated by dilating the cervical canal, otherwise the patient recovered in a perfectly satisfactory manner.

Remarks.

The chief points of interest in this case are the peculiar developments of the myomatous tumor from the posterior surface of the uterus and its extension into the cul-de-sac; the upward displacement of the bladder covering the whole anterior surface of the uterus, and the method of attacking such a tumor.

Such a growth is rarely seen, and, therefore, this method of operation will only be useful in a certain number of abnormal cases. The principle, however, would seem to me to be a good one, and it might also be applicable in other conditions besides cases of posterior myomatous development. Thus, for instance, in densely adherent pelvic structures, or in cases with large pelvic abscesses, it would be easier to separate the bladder from the uterus anteriorly where there are usually but few adhesions, and to tie the uterine arteries on each side before any attempt is made to remove the adherent masses, thus obviating one of the chief difficulties in such an operation, namely, hæmorrhage from the misplaced or with difficulty accessible uterine artery.

The cervix, in these cases, could be cut across after tying the vessels, and a point of leverage obtained to remove more easily the adherent structures.

A SQUAMOUS-CELLED CARCINOMATOUS DEGENERATION OF AN OVARIAN DERMOID CYST; ALSO AN ADENOCARCINOMA OF THE OVARY, ASSOCIATED WITH AN OVARIAN DERMOID CYST.

By Lindsay Peters, M. D.

(*From the Gynecological Department of The Johns Hopkins Hospital.*)

Out of 7,600 patients admitted to the wards of the Gynecological Department of the Johns Hopkins Hospital since September, 1889, (there being 42 cases of dermoid cysts among that number), only two cases of carcinoma associated with a dermoid cyst have been observed. There was one case of dermoid cyst of the ovary coexisting with squamous-celled carcinoma of the cervix uteri, the latter extending out into the broad ligaments and to the tubes, not, however, involving the dermoid cyst. The combination of carcinoma and dermoid in the same tumor in any manner is rare, and carcinoma developed primarily from epithelial structures in a dermoid is very seldom seen.

In discussing the relations of carcinoma to dermoid cysts it is necessary to bear in mind the various possibilities, which are: First, a carcinomatous degeneration of the dermoid tumor itself; second, the carcinomatous degeneration of a part of an ovary, another part of which contains a dermoid cyst; third, the original association of a multilocular cyst with a dermoid cyst, followed by a carcinomatous degeneration of the multilocular tumor, (Gessner), and fourth, the possibility of a dermoid cyst of the ovary being invaded by a carcinoma from some contiguous organ.

The first case to be described in this report is one of carcinomatous degeneration of an ovarian dermoid cyst. Dr. Kelly

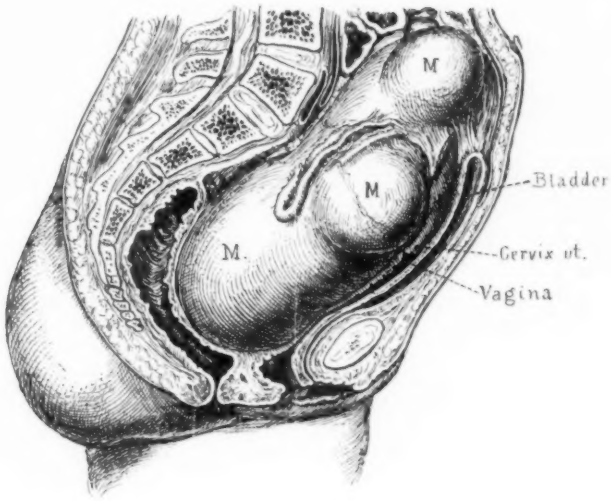

FIG. 1.—Shows the relations of the tumor to the rectum, bladder, and symphysis pubis and its extension into the cul-de-sac.

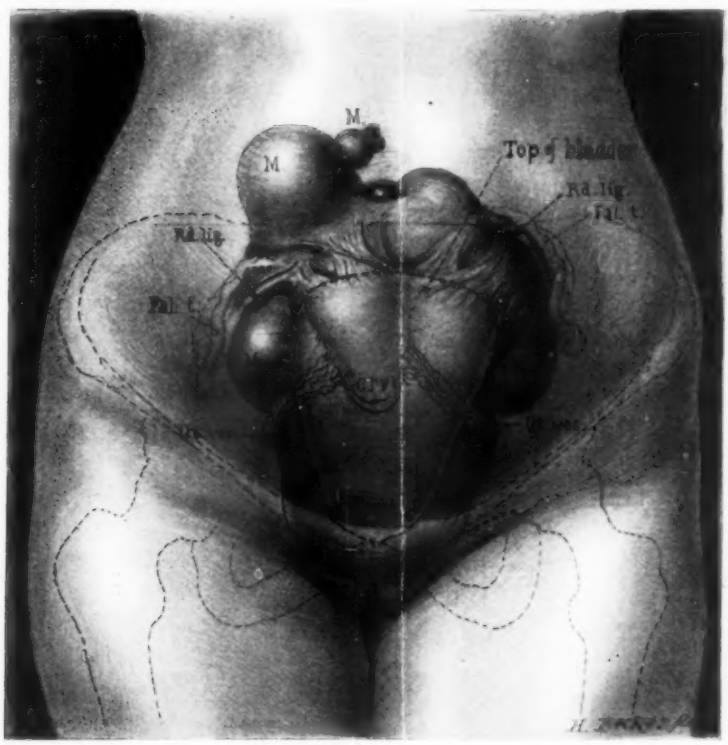

FIG. 2.—Tumor as it would appear through the transparent abdominal wall, showing diagrammatically its relations to the surrounding structures. The relations of the bladder to the cervix and body of the uterus can be well seen.

has already reported this case briefly before the Medical Society of the Johns Hopkins Hospital,* and I shall, therefore, not dwell upon the points which he has brought out, but shall endeavor to add to what he has reported something of the subsequent history of the case, and a more detailed description of the pathological findings. I am indebted to Dr. Kelly for placing the case in my hands for thorough description and publication.

Case I. (*Gynecological No.* 7394).—Mrs. H. T., white, aged 46 years, was admitted to the Johns Hopkins Hospital, Nov. 24, 1899.

Complaint, "pain in bowels."

The patient has had 10 children, no miscarriages. There is nothing of interest in the history of her labors except that she had puerperal septicæmia after the birth of her 9th child, 14 years ago, and that the birth of her last child, 10 years ago, was induced at the 8th month on account of hæmorrhages which began in the 6th month of gestation and ceased soon after delivery.

Menstruation has always been regular and normal. The last menstruation before operation was on Nov. 4, 1899.

She has had slight leucorrhœa, from time to time, for many years.

Her family history is good, excepting that her mother died of heart disease.

Her past history is good.

The history of her present illness is as follows. Since the birth of her 9th child, 14 years ago, she has suffered with soreness in both inguinal regions, and with distressing bladder symptoms—a sensation of weight or pressure on the bladder and, at times, incontinence of urine, at other times prolonged and painful retention of urine. Seven or eight years ago she noticed for the first time a tumor low down in the left side of the abdomen. This was freely movable and changed its position whenever the patient assumed certain postures. She thinks that the tumor remained the same size from the time she first noticed it until about three months ago, when it seemed to rise and cause "knots" or "lumps" in the abdomen. About this same time (three months ago), having previously been able to go about and attend to her duties, she took to her bed on account of the severity of the bladder symptoms mentioned above, and has remained in bed ever since. For the past two weeks she has been unable to void urine, except a very little at a time, and that only while standing.

Physical examination on admission.—The patient is emaciated; her cheeks are sunken, the complexion is sallow, the eyes watery, the mucous membranes pale, the tongue clean.

The pulse is regular in force and rhythm, of fair volume, but rather low tension, 96 per minute. The vessel-wall is palpable.

The lungs are negative.

The heart is also negative.

Vaginal examination.—The external genitalia are normally developed, but somewhat atrophic. The vaginal outlet is markedly relaxed. The posterior vaginal wall presents at the vulval orifice over an area of about one square inch. The cervix cannot be distinctly outlined, but is apparently pushed upward an inch or two above the upper border of the symphysis, and to the right side. Here a small polyp can be felt. Filling the whole of the pelvis and extending to within 1½ in. of the vulval orifice, pushing forward the posterior vaginal wall, is a tumor mass. This is in places hard and firm, in other places fluctuant. It is apparently firmly fixed in the pelvis, especially on the right side. The rectum is pushed well to the left side of the pelvis and its lumen is encroached upon by the mass. The uterus is apparently situated upon the anterior face of the tumor, its fundus being about 10 to 12 cm. above the upper border of the symphysis. The bladder is greatly distended, extending to the top of this mass which we consider to be the uterus. During examination urine passes freely from the meatus. The tumor, which apparently springs from the right side of the pelvis, extends to the umbilicus above. It is irregular in outline, somewhat nodular. It is fluctuant and tense over most of its surface and is apparently firmly fixed in the pelvis. Slight crepitation can be felt over the left anterior surface of the tumor.

Operation (*Cystectomy by Dr. Kelly*).—A median incision, 18 cm. long, was made, exposing the uterus flattened against the anterior abdominal wall. Several small, hard nodules in the bladder peritoneum were excised, and others were seen over the peritoneal surface. The tumor was densely adherent to the sigmoid, rectum and pelvic walls. A large leash of blood-vessels running in the infundibulo-pelvic ligament on the left were ligated and cut. The tumor contents (dermoid) were drawn off by a large trocar. The peritoneal coat of the tumor was incised and the tumor-wall separated, by blunt dissection along the surface of cleavage, from its adhesions to the intestines, pelvis, etc. There was moderate oozing until, on detaching the tumor from the rectum and vagina, low down on the posterior wall of the pelvis, near the anus, a carcinomatous mass was encountered, which bled freely and was curetted away. After curettage, removing about 12 cc. of friable material, resembling an advanced cervical cancer, an opening into the posterior vaginal vault was made with the end of blunt forceps and stretched the full width of the vagina for drainage. Washed-out iodoform gauze was laid in the pelvis and brought out into the vagina. The question then was, how to protect this cancerous area, sure to break down immediately, from the peritoneal cavity above. This was done by taking the large, somewhat plastic uterine body, with its right tube and ovary amputated, but with the left tube and ovary intact, and drawing it back into retroflexion, when it snugly and exactly filled the opening at the pelvic brim. The uterus was then sewed to the brim of the pelvis by continuous catgut suture, beginning with the right round ligament and suturing it for about 2 cm. to the brim and then continuing on around the fundus on a line between the tubal ends, anterior to the amputated surface on the right, over to the opposite tube and ovary and beneath them, leaving them projecting up into the abdominal cavity. The rectum was protected from sutures by a thick fold of membrane left from the capsule of the tumor. After extirpation, the rectum just had snug room at the brim of the pelvis. The left round ligament was not sutured, as the suturing ended with the infundibulo-pelvic ligament. Several bleeding points on the sac-wall were ligated. The abdomen was flushed out with normal salt solution and closed with interrupted silkworm-gut and catgut sutures.

Description of the Tumor.—*Gynecological-pathological No.* 3647.

Gross description.—The specimen consists of a cyst, a Fallopian tube and numerous small scraps of tissue of irregular shapes, which were removed by curettage from the posterior wall of the pelvis.

The cyst is 13 cm. in diameter. Exteriorly it is pinkish-yellow in color and for the most part smooth, though in places, especially towards the base, dense adhesions are seen. Also near the base, on the right, postero-inferior portion of the outer surface, is a circular, rough excrescence, about 5 cm. in diameter and raised about 5 to 7 mm. above the surrounding surface. This is composed of pale-pink, somewhat hard, coarsely granular tissue, some parts of which are quite friable, other parts firmly held together by a stout fibrous

*Philadelphia Med. Journ., 1899, Vol. IV, No. 36, p. 1208.

network. At about the centre of this circular area there is a small opening, 5 mm. in diameter, into the cyst-cavity, apparently made by tearing of the cyst-wall in removal of the tumor. There is another small opening, about 2 5 cm. long, in the upper wall of the cyst, made during the operation for the purpose of evacuating the contained fluid. The thickness of the wall varies from 1 to 4 mm., except in one part of the cyst near its base, where long, high, narrow ridges of tissue, to which wisps of long, fine, blonde hair are attached, project into the cyst-cavity. The thickness of these ridges from side to side varies from .5 to 1 cm. They rise from 1 to 2.5 cm. above the surrounding surface and are from 2 to 4 cm. long. The wisps of hair are matted together by a large amount of greasy, sebaceous secretion. In the wall, beneath the base of the highest of the ridges of tissue just described, there is found a mass of hard bone, about 2 cm. in its greatest diameter, of very irregular shape. There are also, on various parts of the inner surface, smooth, slightly elevated ridges which represent the remains of previously existing septa. The remainder of the inner surface has a puckered or rugous appearance and, in general, is of an opaque, yellowish-white color. But there are numerous areas from 3 mm. to 2 cm. in diameter which are very sligh ly (scarcely .5 mm.) elevated, of a reddish-brown color and have sharply defined, circular or irregular outlines. They have a somewhat velvety appearance owing to numerous minute, columnar and papilla-like projections of which they are composed. The inner surface of the cyst opposite the rough, circular area on the outer surface is comparatively smooth, except immediately around the small opening at the centre of the rough area, where there is a border about 2 to 3 mm. in diameter, composed of slightly raised, coarsely granular tissue.

The Fallopian tube is 5.5 cm. long, having a practically uniform diameter of 6 mm. It is enveloped by dense adhesions. The fimbriæ are matted together, the ostium abdominale occluded. Just below the tube, between the layers of the broad ligament, 1 cm. from its outer extremity, are three small, thin-walled, translucent cysts, side by side, 3 to 5 mm. in diameter.

The irregular pieces of tissue removed by curettage are firm in consistency, dark red in color, for the most part very friable, and have many slender projections on their surfaces. They vary from 1 to 2.5 cm. in greatest diameter.

With the exception of the scraps of tissue removed by curettage from the posterior wall of the pelvis, which were preserved in a 5 per cent solution of formalin, the gross specimen was preserved in Müller's fluid and afterwards washed in running water, then placed in 95 per cent alcohol. Sections were cut for microscopic study from (*a*) the ridges of tissue from which the wisps of hair took origin; (*b*) various parts of the wall, not including the rough excrescence on the outer surface; (*c*) the portion of the wall occupied by the rough excrescence; (*d*) from the scraps of tissue curetted from the posterior wall of the pelvis; (*e*) from the Fallopian tube. These, after being properly hardened by the usual method, were embedded in celloidin. Microtome sections were then cut and were stained with hæmatoxylin and eosin.

Microscopic description. (*a*). Sections through the ridges of tissue from which the wisps of hair took origin are seen to have very uneven surfaces, presenting alternate, irregular projections and depressions. Upon the surface is a layer of stratified squamous epithelial cells, which varies from 2 or 3 to 6 or 7 cells in thickness. The most superficial of these epithelial cells have degenerated and have been cast off from the surface either singly or in homogeneous, deeply eosin-stained bands formed by the coalescence of the superficial cells. Definite prickle-cells are seen in the deepest stratum of the layer. In many places the epithelium covering the surface is degenerated throughout the thickness of the layer, being converted into a mass of refractile, disintegrated, deeply eosin-stained tissue. In the stroma beneath the layer of surface epithelium there are many cross and oblique sections of hair follicles and numerous normal sebaceous and sudoriparous glands. Some of the hair follicles contain hairs, others do not. The stroma is composed of dense, wavy fibrous tissue, poor in nuclei, and running through it are many thin-walled blood-vessels. There are also many masses of colored blood-corpuscles in the stroma, some of which are free in the tissues, others contained in the walls of congested blood-vessels. The tissues, in many places, show beginning hyaline change. Scattered through all the tissues of the wall are fairly numerous small round cells and a few polymorphonuclear leucocytes. The degree of the leucocytic invasion varies very much in different parts of the specimens, being quite dense in many places near the inner surface.

(*b*). On examining many sections from various parts of the wall (not including the rough excrescence on the outer surface), it is found to be composed for the most part of dense fibrous tissue which, in many places, shows hyaline degeneration. In a few places, small bundles of non-striated muscle-fibres are seen. The fibrous tissue is densest next to the outer surface, where, in some places, its appearance is suggestive of ovarian stroma. The outer surface is generally smooth and even, but here and there thick, non-vascular tags of adhesions are seen. There are also a few slit-like spaces just beneath the outer surface lined by a single layer of flattened, endothelial cells. Blood-vessels of considerable size are scattered in moderate abundance through all parts of the wall.

The inner surface is, for the most part, devoid of any epithelial lining, although in some places it is covered by layers of stratified epithelium from 2 or 3 to 15 or 20 cells in thickness. The cells in the thickest layers are, in general, flattened from side to side instead of from above downward, as in the stratified squamous epithelium of normal structures such as the cervix uteri, vagina, skin, etc. In the thinnest layers they are flattened from above downward, and in the layers intermediate in thickness they are much less compressed, *i. e.*, more polyhedral in form Some of the cells in the deepest strata are prickle-cells. No definite papillæ are formed beneath the epithelium. The portions of the inner surface not covered by epithelium are wavy in outline and composed of fibrous tissue, which, in many places, resembles chronic granulation-tissue, containing many very small, well-formed, congested blood-vessels. The tissues, a short distance below the surface, are permeated by extravasated blood.

The reddish-brown, slightly elevated areas on the inner

surface, noted in the macroscopic description, are seen in the microscopic specimens to have very uneven surfaces, presenting many irregular depressions and processes. They are composed of loosely disposed cells, which are exceedingly multifarious in size and structure. Some of the cells are of moderate size, polyhedral in shape, containing single, spherical or oval nuclei, which stain homogeneously. There are a few elongate cells with spindle-shaped nuclei, but the most conspicuous feature in the tissues of these areas is the presence of immense giant-cells, some of which occur in groups of from 2 to 5, and appear to be partly fused with one another. They are seen sometimes on the surface, sometimes a short distance below it. Each giant-cell contains from 3 or 4 to 40 or 50 small spherical nuclei, which are grouped around the periphery in some of the cells, towards the centre in others. Numerous minute blood-vessels, many of them engorged with blood, run in and out among the cells, and in the interstices of the tissue are large numbers of small round cells, polymorphonuclear leucocytes and colored blood-corpuscles. The protoplasm of the cells containing single nuclei, as well as that of the giant-cells, is deeply stained with eosin, and has an homogeneous, cloudy, blurred appearance, the outlines of the cells being as a rule ill-defined. The deepest portion of this tissue is continuous with underlying hæmorrhagic areas in the cyst-wall. Its cells show no evidence of abnormally active proliferation, nor any tendency to strike downward into the subjacent tissues.

(*c*). Sections through the part of the wall occupied by the circular excrescence on the right, postero-inferior portion of the outer surface have the following appearances:

The distance from the inner to the outer surface in the sections varies from .5 to 1 cm. The outer portions of the wall are composed mostly of masses of epithelial cells. These masses are very irregular in shape, of various sizes, and are separated from one another by dense fibrous stroma. The epithelial cells in the masses are very variable in form and size, the average-sized cells being about as large as the cells seen in the stratum granulosum of the skin. In general, the cells on and near the margins of the masses are smaller, more closely packed together, and contain more deeply stained nuclei than the cells nearer the centres of the masses. The cells near the central portions of the masses are very large and their nuclei are somewhat more palely stained than those near the margins. All of the nuclei vary greatly in intensity of staining. They also, like their containing cells, are very variable in size, some of them being as much as 5 or 6 times larger than the average-sized nucleus. They are, as a rule, spherical or ovoid in shape, consisting of an outer, narrow, homogeneous, pellucid, lightly hæmatoxylin-stained rim or capsule and a large, central mass of coarse, highly refractile, deeply hæmatoxylin-stained granules, in a few of them a central, spherical or ovoid nucleolus being seen. The protoplasm of the cells is finely granular and stains deeply with eosin. In some places, where the outlines of the cells are distinctly seen, prickles are observed around the margins of the cells. There are many large, necrotic areas in which no cellular elements are found. Small areas of necrosis are often seen in the central portions of the epithelial masses.

The masses of epithelial cells just described have the arrangement and other characteristics of carcinoma; they are, in fact, "carcinoma cell-nests." The new growth, although involving chiefly the outer layers of the cyst-wall, is found (in sections through the wall made in such a way as to include the rough margins of the small opening on the inner surface, opposite the centre of the circular excrescence on the outer surface) to extend through the entire thickness of the wall, in one place a transition from the lining epithelium into the carcinomatous tissue being seen. The only carcinomatous portion of the inner surface is that covered by the rough margins of the small opening opposite the centre of the excrescence on the outer surface. The carcinomatous tissue is seen undermining the lining epithelium as well as growing downward from the inner surface. The growth spreads more and more laterally as it approaches the outer surface.

The portions of the sections not invaded by the carcinoma are composed of dense fibrous tissue. All of the tissues are diffusely infiltrated with leucocytes—chiefly polymorphonuclear. The infiltration is most marked in the fibrous stroma around the cell-nests.

In these sections no karyokinetic figures are found. There are, however, a considerable number of tumor-cells, in each of which a pair of nuclei is seen. Each nucleus in every pair has the form of one-half of an ovoid which has been divided at a right angle to its long axis, the divided ends facing each other and being almost, if not quite, in contact. Except for their form and their position relative to each other, these twin nuclei do not differ in appearance from the nuclei of the tumor-cells in general, nor is any difference between the appearance of the protoplasm of the cells containing the twin nuclei and that of the cells containing single nuclei detected. In addition to the twin nuclei, one occasionally sees a nucleus with a faint, indefinite, light line running across its middle. Some cells are found in which there are three distinct, well-formed nuclei, which are closely adjacent to one another, their adjacent edges being flattened as if from pressure against one another, and a few cells are seen in which there are indistinct lines of cleavage (?) in each nucleus, dividing it into four parts. Still another type of cell is seen which is always mononuclear and is noteworthy, not on account of any peculiarity of its nucleus, but because there are light lines radiating from the margins of the nucleus through the protoplasm to the borders of the cell-wall. These cells are always nearly exactly circular in outline, and their protoplasm stains deeply with eosin in a narrow zone immediately around the nucleus, from which the color gradually shades into a very pale pink at the margins of the cell.

Occasionally one finds a group of cells arranged in concentric layers around a central cell, all the cells in the layers being flattened towards the centre of the group. They have the appearance of "carcinoma pearls" in an early stage of formation.

(*d*). In the sections from the scraps of tissue curetted

away from the posterior wall of the pelvis, the same tissue-elements are found as were described for the outer part of the wall in the third group of sections (*c*), and the tissues have the same general arrangement into epithelial masses surrounded by dense fibrous stroma. The epithelial cells, however, differ from those described under group (*c*) in the following respects: the former have a smaller average size than the latter, their protoplasm stains a faint pinkish-violet color instead of taking an intense eosin stain and their nuclei, instead of being composed of coarse granules are vesicular, having very thin walls containing fine, loosely scattered granules of chromatin. Many of the cells in these sections contain karyokinetic figures showing various stages of indirect cell-division, some of the figures being symmetrical, others asymmetrical. Also many cells are found containing 2 or sometimes 3 well-formed nuclei within a single cell-wall which shows no evidence of beginning division. All of the tissues are diffusely infiltrated with polymorphonuclear leucocytes and small round cells, the infiltration being most marked in the fibrous trabeculæ between the epithelial masses. There is no suggestion of a glandular arrangement of the cells.

(*e*). The folds of the mucosa of the tube are normal in size and are not adherent to one another. They are covered by a single layer of normal, low-columnar, ciliated epithelial cells, which contain spherical or oval, evenly stained nuclei. The stroma of the folds has the normal appearance and is free from leucocytic infiltration. The muscular coats are atrophied, appearing in small, scattered strands of non-striated muscle-fibres just exterior to the tubal mucosa. Between the scattered strands of muscle-fibres is dense, wavy, fibrous tissue, poor in nuclei. The outline of the outer surface is generally slightly wavy and is partly covered by small cells, in a single layer, which have large, oval nuclei, flattened from above downward, which almost completely fill the cells. These are endothelial cells of the peritoneum. There are a few tags of old, slightly vascular, fibrous adhesions projecting from the outer surface.

Deductions from Description of Specimen.—From the above description it is evident that we are dealing with a squamous-celled carcinomatous growth in the wall of a dermoid cyst. As a transition from the lining epithelium of the cyst into the carcinoma is demonstrable in the microscopic specimens and, moreover, there being no discoverable carcinoma in any other part of the body, there can be no doubt that the origin of the growth was from the lining epithelium of the cyst. The fact that the growth at its point of origin covers such a small area and projects so slightly into the cavity of the cyst is remarkable, and we offer as an explanation thereof the suggestion that the pressure exerted by the contents of the tensely distended cyst may have prevented the growth of the tumor into the cavity.

Concerning the peculiar appearances in some of the tumor-cells noted in the description of group (*c*) of the microscopic specimens, it is impossible to arrive at any conclusions, the tumor not having been placed in the fixing fluid until several hours after its removal from the body. However, we think it possible that the appearances are due to changes in the cells which have taken place after extirpation of the tumor, the nuclei in groups of 2, 3 and 4 being possibly the result of the completion of the cycle of division by nuclei which, at the time of removal of the tumor, had already begun to divide. The appearance of some of the multinuclear cells is, however, very suggestive of direct division of the nuclei.

The giant cells noted in the description of group (*b*) of the microscopic specimens have the same appearance as the giant cells which are often met with on the inner surfaces of dermoid cysts free from any malignant new growth. These have been described (Hildebrandt[1]) as foreign-body giant-cells, supposed to be due to the presence of hairs in the walls of the cysts; but we have often observed them in parts of the walls of dermoid cysts in which there were no hairs to be seen and also in simple dermoids in which no hairs were found in any part either by macroscopic or microscopic examination; they are, therefore, as suggested by Cullen, more probably a form of embryonic epithelium from which the lining epithelium of the cysts is developed. In the case which we now have under consideration the giant-cells are found in parts of the tumor remote from the ridges of tissue to which alone the hairs were attached.* The tissue in which some of our giant cells are embedded is, in all probabilty, granulation tissue formed as a result of long-standing inflammation of and hæmorrhage into the tissues upon and immediately beneath the surface of the cyst-wall.

Post-operative History.—The patient had practically no nausea after operation, but pain during the first 3 days was sufficiently severe to require morphia. During the 5th, 6th and 7th days the gauze drain in the pelvic cavity was gradually pulled out, a small piece of it being clipped off each day, until on the 8th day all that remained of the drain was removed, after which a considerable amount of sanguino-purulent fluid escaped. The cavity in the pelvis was then carefully cleansed by douching with a saturated solution of boracic acid and again filled with clean gauze. From this time on dilatation of the opening into the cavity and douching and repacking of the cavity were repeated every day. On the 9th day the abdominal wound was inspected and found to have healed perfectly. Alternate silkworm-gut sutures were removed. On the 12th day all remaining sutures were removed from the abdominal incision, and the following note was made. "By examination with one finger in the cavity and another finger in the rectum, it is ascertained that the cavity lies entirely to the right of the rectum and is separated from it by a septum of firm, indurated tissue, about .5 cm. thick, which extends upward (along the side of the rectum) to a point just within the reach of the examining finger. The lumen of the rectum is considerably encroached upon."

The patient was allowed to be out of bed in a wheel-chair on the 24th day, and was able to walk several days before her discharge from the hospital on the 36th day.

During the entire convalescence there was considerable

* Cullen says that in very early dermoids of the ovary, where no epithelium is as yet present and where no sebaceous nor sudoriparous glands are found, the diagnosis can be made, with almost absolute certainty, from these characteristic giant cells. (*Personal communication*).

sanguino-purulent discharge, which at times had an offensive odor. The patient complained repeatedly of pain in the right hip and back, chiefly at night. There was also, at times, severe pain in the rectum, which was, however, relieved by defecation.

During the first 3 days after operation the temperature chart showed a range of temperature between 100° and 101°F., the pulse ranging between 96 and 108 per minute. After this time the temperature continued very slightly above normal until the end of convalescence, except on the 19th and 24th days, when there were slight rises to 100.5°F. The pulse, after the 3rd day, ranged between 88 and 104 per minute.

The following is a note made on the discharge of the patient from the hospital on the 36th day. "The cavity posterior to the vagina has decreased in size. It holds about two ounces. The new growth has increased markedly and extends down to the anal orifice. The opening into the cavity admits the index finger. The uterus is felt in adherent retroflexion. The patient's general condition is only fair; she suffers considerable pain in the hip and back; she also requires codeia at night for sleep, and suffers with constipation."

In a letter written thirteen weeks after operation, the patient states that she notices very little change in her general health since leaving the hospital, but that she now has a very offensive discharge, "like decayed blood," from the rectum. It is, therefore, highly probable that the carcinoma has now extended through the rectal wall. The fact that the patient is still alive and notices very little change in her condition, except that which can be explained by local extension of the growth, shows that the efforts to protect the abdominal cavity by suturing the uterus to the pelvic brim have been successful.

REVIEW OF THE LITERATURE.—The first indubitable case of carcinoma developed from epithelial elements of a dermoid cyst is that reported by Bierman,[2] in 1885. Before that time other cases had been published by Heschl,[3] von Wahl,[4] Cohn,[5] Veit[6] and Pomorski,[7] in which carcinoma and dermoid cysts were said to be associated in the same tumor; but none of these will be discussed, some of them being too inadequately reported to establish their authenticity, others undoubtedly deserving to be considered as "mixed tumors" and not as dermoid cysts which have undergone carcinomatous degeneration. In 1884, Babinski[8] reported two cases which he considered to be carcinoma "*probably*" derived from dermoid cysts, but his descriptions are meagre and his conclusions are uncertain. After the publication of Bierman's case, Himmelfarb,[9] in 1886, Krukenberg,[10] in 1887, and Tauffer,[11] in 1895, each reported an authentic case of squamous-celled carcinomatous degeneration of a dermoid cyst. In 1897, two other cases were published, one by Thumin,[12] another by Yamagiwa.[13] Clark,[14] while working in the laboratory of Chiari, at Prag, published, in 1898, the case of a dermoid cyst which had been discovered among a large collection of museum specimens and which proved, on microscopical examination, to have undergone carcinomatous change in one part. The tumor had been extirpated by abdominal section, in May, 1885, from a woman aged 29 years. At the same operation a metastatic nodule the size of a walnut was removed from the left axilla. The patient made a good recovery from the operation, but no further history was obtainable. Clark was able to trace, in the microscopic specimens, a transition from the normal epithelial lining of the cyst into the carcinomatous tissue. He also described giant-cells similar to those which we have noted in our case. Tauffer gives very full abstracts from the descriptions of the cases of von Wahl, Heschl, Bierman, Himmelfarb and Krukenberg, and Clark also gives a very satisfactory summary of all the cases published prior to his own.

Since the report of Clark's case, we find only one other observation of carcinomatous degeneration of a dermoid cyst of the ovary, that reported by Lockhart and Anderson,[15] in 1899. In their case the patient was an unmarried woman, 50 years of age. At operation, the tumor was punctured and "120 ounces of thick, grumous fluid, containing caseous material and hair," escaped, revealing the dermoid nature of the tumor. It was learned that the tumor had originated in the left ovary, and that its pedicle, consisting of the uterus and broad ligament, was twisted half way around. Many dense adhesions of the cyst to the upper part of the left wall of the abdomen, to the omentum, to the under surface of the right lobe of the liver, to the right anterior abdominal wall and to the intestines, were encountered. The patient did well for the first four weeks after operation, and was discharged from the hospital on the 31st day, but died one week later. The tumor is described as a "large, irregular-shaped mass, measuring 18 x 15 x 14 cm., weighing 1,570 grms." Its peritoneal covering was "thickened and hæmorrhagic." On section it was found to be composed of a "series of large cysts whose walls were markedly thickened, in some places measuring 5 cm." The cyst contained a "thick, oily, flocculent fluid, as well as two large, rounded masses of hair, about the size of large apples." Three teeth, embedded in the wall and projecting into the cyst-cavity, were also found. The following is a copy, in full, of the description of the microscopic specimens: "The tumor is seen to be composed mainly of epithelial elements, which infiltrate extensively the fibrous tissue stroma. Multiple pearl-nests are found in these areas. At other points the epithelial cells are arranged in alveolar and tubular forms, as in carcinoma, with large bands of fibrous tissue surrounding them. A large amount of adipose tissue is also present. The vessels throughout are numerous, and engorged with blood, and in places surrounding these are a large number of small, round cells." They then conclude:

"The tumor is, therefore, an ovarian dermoid cyst, with epitheliomatous, and, in some places, carcinomatous infiltrations. It also shows evidences of acute, and, in some places, sub-acute inflammatory reaction."

Cone,[16] in 1897, described a dermoid of the lower jaw which showed squamous-celled carcinomatous degeneration, and referred to similar cases observed by Franke, Czerny and Briddon. Cone also noted in his case the presence of giant-cells. These were of two kinds, one of which were found around the roots of hairs and thought to be "foreign-body giant-cells," the other kind being seen in the centres of typical tubercles and considered as "tubercle giant-cells."

In 1897, Yamagiwa published, with his case, which we have

already alluded to, another case which he believed to be one of adenocarcinoma, developed from a nipple-like growth or anomalous, misplaced mammary gland on the inner surface of the dermoid cyst. That is the only case of adenocarcinomatous degeneration of a dermoid of which we are able to obtain record.

As yet, no case of carcinoma, thought to be derived from the sudoriparous or sebaceous glands of a dermoid cyst, has been reported.

The secondary changes, other than carcinomatous, which have been observed in dermoid cysts, are rather limited in variety. Friedländer[17] has reported an instance of cystic degeneration of glands in the wall of a dermoid, Bierman[18] an instance of primary sarcoma and Faquet[19] an instance of endothelioma in a dermoid. Papillary growths in multilocular ovarian cysts, which were only partly dermoid, have also been reported.

The remaining case which we have to report is interesting as an example of the second class of possibilities which we have mentioned, *i. e.*, a carcinomatous degeneration of a part of an ovary, another part of which contains a dermoid cyst. On looking through the literature we do not find any similar case previously reported.

Case II. (*Gynecological No.* 5164.)—Mrs. K., white, aged 36 years, was admitted to The Johns Hopkins Hospital, April 6, 1897.

The patient has had 6 children and 1 miscarriage. Puerperal fever followed her last confinement, six years ago, and at the same time she had "milk leg," affecting the right lower extremity.

Her menses began at 16 years. They are always regular and last 3 to 4 days.

She had profuse and offensive leucorrhœa for two years after the birth of her last child.

Two uncles died of phthisis. The family history is otherwise negative.

The patient has had only the usual diseases of childhood, and has always been strong and well.

Her present illness began in August, 1896, with fever which her doctor pronounced typhoid. She was in bed two weeks and since then has had fever "off and on," and at recent menstrual periods has suffered exquisite pain in the left ovarian region, with great nausea and vomiting.

Operation (*Double Cystectomy, with removal of the uterus*, by Dr. Kelly).—The right ovary is found converted into a lobulated and nodular tumor about 10 cm. in diameter. This is slightly bound down by adhesions, and at its inner and upper pole is a subperitoneal cyst, 4 cm. in diameter.

Enucleation was commenced on the right side on account of adhesions of the left ovary, which was twice the normal size and was occupied by a growth similar to that on the right. The uterus was amputated at the cervix, and the operation was then completed in the usual way. Small, secondary nodules were seen in the omentum.

Over the region of the left kidney there was a lobulated, nodular mass about 8 x 7 cm. This was probably infiltrated omentum.

The abdomen was washed out with salt solution. In closing the wound, catgut was used for the peritoneum, and interrupted, through-and-through silkworm-gut and catgut for the other layers.

Description of the Specimen. *Gynecological-pathological No.* 1645.

Gross description.—The uterus measures 6.5 x 4.5 cm. The posterior surface and fundus are covered by adhesions. On section the uterine cavity is seen to be 4 cm. long, and 4 cm. broad at its fundus. The uterine mucosa is pale and looks œdematous. In the cervix is a dilated follicle 4 mm. in diameter.

Right side.—The ovarian tumor, which resembles a cystic kidney in contour, measures 10 x 5.5 x 4 cm. The surface is nodular, and on one side is a bunch of 8 or 9 cystic or partly-solid nodules, some of which resemble hæmorrhagic Graafian follicles, others contain clear fluid. On section, the tumor is found to be of a yellowish color and to consist of a somewhat friable, homogeneous or fibrillated tissue, which here and there, around the periphery, presents small cystic areas into some of which hæmorrhage has occurred. In the hilum of the tumor is a cyst 2.5 x 1.5 cm. which contains a buttery material resembling dermoid contents.

The Fallopian tube is bound down to the surface of the tumor, but is apparently patent.

Left side.—The ovary is converted into a small, nodular tumor, 4 x 3 cm., resembling the one on the opposite side. On its upper surface, at the inner pole, is a corpus luteum 1 cm. in diameter.

Microscopic examination.—The uterine mucosa has an intact surface epithelium. The glands are abundant and a few slightly dilated. Frequently a gland is seen extending a short distance into the muscular coat, but the glands are perfectly normal. The stroma of the mucosa is rarefied.

Right side.—The ovarian elements are almost entirely replaced by neoplastic tissue. This consists of narrow, branching processes of epithelium penetrating the stroma in all directions. These processes often consist of but two rows of cells, which may present a narrow central lumen. Frequently, however, the cells form solid cylinders, sometimes of considerable thickness. On cross-section, solid nests of epithelial cells are found or a minute cavity, lined by one layer of cells. The individual cells vary in size and form, but are usually large, oval or cuboidal, and contain large, round, oval, crescentic or irregular nuclei, which in general take an intense, solid stain. Nuclear figures, both symmetrical and asymmetrical, are abundant, and there is slight karyorhexis, but, on the whole, nuclear fragmention is not notable, and cell degeneration of all kinds is practically absent. The cell-masses are separated from one another by delicate strands of connective tissue, but the tumor is further irregularly divided into lobules by broad bands of connective tissue, and by practically unaltered ovarian stroma, which, in some portions, especially around the periphery of the tumor, is present in considerable amount, though in every part showing, here and there, small epithelial masses.

The cystic portions appear to have originated in Graafian follicles or degenerated corpora fibrosa. In one section a corpus fibrosum is found. Scattered through the stroma are a moderate number of small round cells. The vascularity of the tumor is moderate, the vessels usually of small size.

The cyst found in the hilum of the tumor presents the usual appearances of a simple dermoid. It is lined by stratified squamous epithelium, and in its wall are a few sebaceous

glands. No hair follicles are seen. For the most part the cyst is surrounded by a narrow band of connective tissue or ovarian stroma, but at some points the epithelial cells have penetrated to the surface and cell-masses are found in the mesosalpinx and even between the layers of muscle-bundles in the tube-wall. The broad ligament also contains metastases, cell-nests being found in the lymph-spaces, and, in one place, in a large vein. The tubal mucosa is normal and no tumor elements are found on the upper surface of the tube-wall.

Left side.—The tumor is similar to that on the opposite side. The corpus luteum observed macroscopically presents the usual features and shows commencing organization.

Diagnosis.—Carcinoma ovarii duplex associated with a small dermoid cyst in the right ovary. Corpus luteum in the left ovary. Practically normal uterine mucosa. Perisalpingitis. Subperitoneal cysts.

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PULMONARY TUBERCULOSIS, WITH DIFFUSE PNEUMONIC CONSOLIDATION, IN A LION.

By W. G. MacCallum, M. D., and A. W. Clement, V. S., *Baltimore, Md.*

While in Birmingham, Ala., in November, 1899, one of the lions belonging to the Hagenbeck menagerie, a large adult-male of the black-maned sort, which had been captured in South Africa and had been in captivity ten years, fell ill. The keeper noticed that the lion was not well and frequently refused food. On the removal of the menagerie to Baltimore it grew worse, developed a slight grunting cough, became very much thinner than normal, and, after an illness of about four weeks altogether, died.

The *autopsy* was performed the next day. The body was that of an adult male lion, said by the keeper to be about fourteen years old. The subcutaneous and omental fat were very much wasted. There was no accumulation of fluid in either peritoneal or pleural cavities, and the peritoneal surfaces at least were smooth and glistening.

For the sake of brevity, the description of the heart and abdominal viscera will be omitted, as they were apparently quite normal. The lungs appeared somewhat collapsed, and seemed to contain much less air than normal. Their pleural surfaces were not quite smooth, but had lost their gloss. There were, however, no adhesions between the layers. The left lung, which consisted of three lobes, was found to contain very little air, small portions of the upper lobe only being insufflated; the middle and lower lobes were quite solid. On cutting through the lung, the cut surface of the upper lobe presented, in general, a translucent appearance, being densely studded with small translucent nodules which projected from the surrounding surface; these hardly exceeded a pin-head in size, and never showed any central area of necrosis. The intervening lung-substance was gray or grayish-yellow, and somewhat gelatinous and translucent. The lower lobes were more firmly and uniformly consolidated, the firmness being due to a diffuse consolidation rather than to the translucent nodules which were more sparsely scattered throughout these lobes. The cut surface was, as in the upper lobe, grayish-yellow and somewhat translucent. In the posterior portion of the lobe, there were two well-defined cavities communicating with one another by a narrow channel, and marked off from the surrounding lung by the fibrous thickening of their walls. These cavities communicated with the bronchi; their walls were fairly smooth and covered with a purulent material. Obliterated arteries crossed from side to side.

The right lung was much more voluminous than the left, the upper lobe being insufflated and containing only a few of the translucent nodules described. The lower lobes, as in the left lung, were consolidated. They were riddled with tubular cavities, which correspond with the bronchi, and which, for the most part, were filled with a yellowish purulent material.

The bronchial glands were slightly enlarged and deeply pigmented, but showed no areas of caseation.

Hardened sections of the upper lobes of the lung show the presence of small areas of consolidation here and there. These consist of rounded or oval tubercle-like masses of cells, sometimes close to the bronchi but more often in relation with the small blood-vessels. They are not entirely without a blood supply, for minute blood-vessels may be seen in their interior. They are made up for the most part of epithelioid cells, with vesicular nuclei arranged in an irregularly concentric manner,

often about several centres. There are very few lymphoid cells, but a considerable number of cells resembling polymorphonuclear leucocytes; and these, with the epithelioid cells, which are often much distorted and of bizarre form, make up the nodule. Very rarely is there any central giant-cell. These nodules are often very sharply outlined on account of the fact that they may fill an alveolus without disturbing the epithelium of the adjacent alveoli. The alveoli adjacent to the tubercles contain a gelatinous exudate consisting almost entirely of coagulated fluid and desquamated epithelial cells. There are a few polymorphonuclear leucocytes, but scarcely any fibrin; occasionally a little is shown by Weigert's fibrin stain.

Sections of the lower lobes show a great increase in the connective tissue throughout the lung, associated with the tubercle nodules, which are here much conglomerated. Giant-cells are seen in these matted tubercles, although so rare in the discrete nodules in the upper lobes. The alveoli of the intervening substance are completely obliterated by the fibrous tissue which is often much pigmented by coal-dust. In other portions of the lower lobes there are areas of gelatinous pneumonia, and also areas in which the walls of the alveoli, together with the exudate, have become completely necrotic and caseous.

The more densely consolidated portions often show definite bronchiectatic cavities, with thick fibrous walls and a content of cellular débris.

The giant-cells described above very commonly contain well-defined tubercle bacilli, as shown in sections stained by the method of Mallory. Stained by Weigert's method no other organisms can be demonstrated. Cultures from the lung were sterile, and two guinea-pigs, inoculated subcutaneously and intraperitoneally with emulsions of the lung substance, unfortunately died from intercurrent infections, so that no propagation of the organism was effected.

The demonstration of bacilli, identical in morphology with the tubercle bacilli in the giant-cells which formed the centres of nodules in the lung, morphologically like tubercles, seems conclusive enough evidence that the lesion was really tuberculosis of the lungs.

Sections of the other organs showed no tubercles and no other noticeable abnormality.

The exclusive localization of the process in the lungs is interesting in connection with the similar case reported by Straus,* in which, although there were large caseous masses in the lungs, there were no other viscera involved.

Straus' case is the only one in the literature which is described in detail. Tuberculosis in lions does not seem extraordinarily uncommon, however, for Jensen mentions two cases, Haughton another, and Rayer, quoting Pirrault, two others. It is well known from the work of Jensen,* Eben,† Froehner,‡ Bollinger§ and others, that dogs and cats are more commonly subject to tuberculosis than is generally thought to be the case.

The localization of the tuberculous lesions in these more or less closely related animals is of interest in connection with this case. Dogs, as reported by these authors, most frequently suffer with pulmonary tuberculoses, and tuberculosis of the serous surfaces is with them more common than in cats, in which, while pulmonary tuberculosis predominates, lesions in the digestive organs are especially frequent.

It is not within the scope of this note to review the literature on tuberculosis in animals, of which good summaries are given by Nocard‖ and Leray,** Rayer†† and others.

Lebert,‡‡ in writing of the tuberculosis of apes, states his opinion that they probably suffer in wild life as well as in menageries, and that they live no better in the tropical menageries than in the more northern ones. General opinion, however, seems to favor the view that confinement so lowers the resistance of wild animals, and especially those transported from tropical countries, as to predispose them to the invasion of the tubercle bacilli.

The most important result of a study of this case is apparently the evidence in favor of the view that a diffuse pneumonic consolidation can be caused by the tubercle bacillus alone. Cultures were sterile, and coverslips and sections showed no organisms except the tubercle bacilli, a condition not often found in the human lung, the seat of so extensive a change.

Whether the peculiarities of the bacilli, so much discussed of late,§§ or the differences in the tissues of the beasts, are to be given as the causes of the slight morphological differences in the tubercles in different animals, must be left undecided here.

* Straus: Arch. de med. exper., 1894, VI, 645.

* Jensen: J. comp. path and therap., 1891, IV, 103.
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ARSENICAL PIGMENTATION AND KERATOSIS.*

By Louis P. Hamburger, M. D., *Assistant in Medicine, Johns Hopkins University.*

This patient, who has been kind enough to appear before the society to-night, is a clerk, forty-two years of age. He entered the Johns Hopkins Hospital Dispensary on the first of November 1899, complaining of swelling of the feet and abdomen. The family history is negative. As a child he had measles and scarlet fever. He has used neither alcohol nor tobacco. To that which is of importance in his past history I shall refer later. His illness began about eight months ago with a "cold" and a cough. About a month thereafter his abdomen began to swell, and he noted that at the end of the day's work his legs were swollen. The cough soon disappeared but the swelling of the abdomen continued. He has had no shortness of breath, nausea, "fainting spells" nor symptoms of weakness. His bowels have been regular. He presented about the same condition when I first saw him that he exhibits now. He is a sparely nourished man, the visible mucous membranes are of good color and present no unusual pigmentation. What immediately attracts one's attention is the condition of his skin. There is a more or less deep-brown discoloration over almost the entire body. The pigmentation as it appears over the abdomen may be taken as a type of this discoloration; differences in degree are presented by the skin in various localities. The skin in this situation is of a mottled yellowish-brown color; the mottling is due to small rounded areas of less pigmented, almost white skin, alternating with similar areas more deeply colored. Here and there are little dark, almost black, mole-like spots. The skin feels natural and is at points a little scaly. The face is slightly involved; it is freckled, the complexion is muddy. On the neck, particularly at the back and the sides, the discoloration is marked, being less punctate and more diffuse than over the abdomen. Still more diffuse is the coloring of the axillary folds; they are uniformly colored a deep-brown. The punctate arrangement is resumed over the shoulders and arms, being more marked over the posterior and internal aspects of the limbs. The discoloration is slight over the forearm and practically absent over the hands. The chest and upper part of back are slightly involved; the areolæ, however, are of a dark chocolate-brown color. The abdomen and lower half of back are markedly pigmented. The inguinal folds, buttocks and internal aspects of the thighs are strikingly dark. Toward the lower thirds of the thighs the pigmentation fades; the skin of the legs is only dotted here and there with spots of pigment; the feet are free from the discoloration.

The skin of the hands is rough and dry. Over the palms it is diffusely thickened. Here, as well as over the dorsal surfaces and between the fingers, are numerous small and large dirty-gray warts and callosities from the size of a pin-head to that of a pea. Some of them look like ordinary warts; others are smaller and more like little fine local thickenings. There is a "wart" on the ulnar border of the right wrist. The nails look natural. Projecting from the left elbow for a distance of about a centimetre is a curious conical wart-like thickening recalling somewhat the heaped-up scales of psoriasis.

The soles present even a more remarkable appearance than the palms. Here too is a diffuse thickening but particularly along the outer border, the heel and area corresponding to the metatarsophalangeal articulations. Over these parts and extending a little way up the posterior aspect of the heels there are numerous yellowish horny excrescences of all sizes, discrete and confluent. The nails are unaffected. From the anterior surface of right shoulder there projected a yellowish-brown, lobulated round wart. It was excised, and, examined microscopically, shows the structure of a papilloma.

Below each internal malleolus is a reddened scaly patch having a diameter of about a half centimetre. They bleed from minute points on removing the scales (psoriasis).

The lungs are clear. The point of the heart's maximum impulse is in the 5th l. i. s. in the nipple line. At this point as well as in the axilla a blowing systolic murmur is heard. The pulse is regular, 62 to the minute.

The abdomen was distended, bulging a little at the flanks. In these regions the percussion note was flat, but became tympanitic on one side when lying on the opposite.

The liver dulness began at the sixth rib in the right parasternal line. Palpation of the abdomen was unsatisfactory owing to the distention. The skin over the shins pitted a little on pressure. The urine contained neither albumin nor sugar.

Under a course of purgation the complaint for which he sought treatment has been a good deal relieved. The abdomen is not so distended, the feet are not so much swollen.

The cutaneous changes had come on so gradually that the patient had paid little attention to them. The warts had been annoying and he had had some of them removed from time to time.

When I saw this combination of extensive pigmentation and keratosis, I made inquiry at once as to the use of arsenic. The patient was much surprised by the question, replying that he had been taking Fowler's solution in doses of from five to eight drops three times daily off and on for a period of ten years. During this time he suffered from a cutaneous eruption which first appeared as a patch on the antero-external aspect of the right knee. It was red, dry and scaly. Other patches of varying sizes appeared from time to time over the body. The eruption itched, bled on scratching, and resembled the "spots" now present on the ankles. Arsenic was prescribed and the skin disease was benefited. After three or four weeks he would discontinue the use of Fowler's solution, only to resume it as a rule in another fortnight; at times because of the

* Presentation of the patient before the Johns Hopkins Hospital Medical Society, December 18, 1899.

[Note.—Since this paper has been in press my attention has been called to the excellent article by Dr. Hartzell on "Epithelioma as a Sequel of Psoriasis and the Probability of its Arsenical Origin," which was published in the *Am. J. of Med. Sc.* of September, 1899. Some of the ground here independently traversed is covered by his contribution.—L. P. H.]

appearance of a fresh patch of eruption, often because of a fear of its return. Just when the present cutaneous manifestations made their appearance he does not know, but he is quite sure that it was subsequent to the use of arsenic.

To recapitulate: This man, suffering from some chronic cutaneous affection (probably psoriasis), began taking arsenic in the usual doses ten years ago and has continued its use off and on ever since. He took the last dose three weeks before his first visit to the dispensary. Then he had ascites and presented the cutaneous lesions which we have just considered.

It is more than probable that there is a causal relation between the ascites and the use of the arsenic. In this patient no other etiological factor is available. Mr. Hutchinson* has described a similar but more severe case in which paracentesis was performed on three occasions, complete recovery following only on discontinuing the drug. And in Geyer's report† on the endemic arsenicism of Reichenstein, due to the arsenical drinking water, several similar cases are quoted. However, it is not to this condition of our patient that I wish to call particular attention, but to the combination of widespread pigmentation and keratosis of the hands and feet. It is a clinical picture of prolonged arsenical medication. So characteristic is it that, in this case, the diagnosis can be made *de visu* without the assistance of the patient's statements.

It is right interesting to know how the relation between these dermatoses and the use of arsenic has been established. I shall begin with a consideration of the melanoderma.

Thomas Hunt is probably the first observer to call attention to arsenical pigmentation. In a communication on the administration of arsenic, published in 1847, he wrote: "The trunk of the patient first, and subsequently all those parts of the body which are by the dress protected from the access of light and air, become covered with a dirt-brown, dingy, unwashed appearance, which under a lens reveals a delicate desquamation of the epidermis, and is, in fact, a faint form of pityriasis."‡ He viewed this change as an effect of the drug's action.

In spite of this early account of arsenical melanoderma the condition was not generally recognized for many years thereafter. It was well known that any chronic inflammation of the skin might leave its mark in the shape of a pigmentation at the site of an old lesion. Hebra, in his well-known textbook, spoke of this fact in connection with cases of psoriasis, and particularly those treated with arsenic, recommending a reduction of the dose as soon as the pigmentation appears.§ No more definite statement regarding the relation between the arsenic and the discoloration is made. Before Hebra's book was published, Devergie had expressed the opinion that the pigmentation in such cases is in all probability due to the arsenic, and the term "taches arsenicales" is applied to the discolored areas.* But this view was not so readily accepted, and discussion continued as to what share the disease took and what rôle the arsenic played in the causation of the melanoderma. In time, however, there accumulated many dermatological observations, in which the pigment was said to appear at points unaffected by the original cutaneous disease, so that there could be no doubt as to its arsenical or inflammatory origin. Finally, when clinicians began to report numbers of cases, chiefly of chorea and accidental poisonings where discoloration of the skin followed the ingestion of the drug, arsenical pigmentation was accepted as an established fact and came to take its place in the list of arsenical dermatoses.† That list is a long one; besides the eruptions which we are now considering, it includes representatives of all the elementary cutaneous lesions from the œdematous to the pustular. In this connection it is of interest to note that a certain chronological sequence in the appearance of these eruptions can be observed. Some represent an acute intoxication, as it were; others, a chronic. At one end of the series stands the œdema which may come on after a day or two's administration; at the other end are the melanosis and keratosis. As a rule, the melanosis appears after a period of some weeks or months of arsenical medication. It matters not what preparation of the drug is used; arsenious acid, sodium arseniate, Fowler's solution—all have caused it.

The localization of the discoloration, as our patient presents it, may be taken as typical. The pigment appears in small yellowish-brown maculæ, which coalescing may come to cover a large area of skin, giving to it a rather characteristic mottling. But it is not always characteristic enough to be distinguished from the bronzing of Addison's disease. Like the pigmentation of this disease, it is more intense in localities exposed to friction or where there is normally more or less pigment. In this patient you see how dark the axillary and inguinal folds and the areolæ are. Unlike the coloring of Addison's disease, the exposed parts do not tend to suffer, nor are the visible mucous membranes involved. The shade of the pigment does not help in the differentiation from "bronzed skin," for in both conditions all shades of brown may be represented. Indeed, a case of arsenical pigmentation has been reported in which the skin, from the groins to the toes, was "absolutely black."‡ When one considers that these patients may present the gastro-intestinal symptoms of arsenic poisoning, the differentiation between arsenical intoxication and Addison's disease becomes worthy of consideration. There is a case of so-called arsenical melanoderma on record which, by its subsequent course, proved to be an example of suprarenal disease.§

The error might have been avoided had the pigmentation of the mucous membranes been rightly interpreted.

In phthisis and exophthalmic goitre pigmentation of the

* Archives of Surgery, 1895, Vol. VI, p. 389.

† Ueber die chronischen Hautveränderungen beim Arsenicismus u. Betrachtungen über d. Massenerkrankungen in Reichenstein. Arch. f. Derm. u. Syph., 1898, Bd. 43, S. 221.

‡ Further observations on the administration of arsenic. Lancet, 1847, I, p. 92.

§ Lehrb. d. Hautkrankh., 1874, 2 Aufl., S. 345.

* Traité pratique des Maladies de la Peau, 1857, p. 137.

† For literature, see Geyer, loc. cit.

‡ Barthelemy: quoted by Rasch, Contribution a l'étude des dermatoses d'origine arsenicale, Ann. de Derm. et de Syph., 1893, t. IV, p. 160.

§ Audry, Ann. de Derm. et de Syph., 1896, t. VII, p. 1415. For "note rectificative," see tome IX, 1898, p. 538.

skin is sometimes seen. It is possible, as has been suggested, that in some of these cases the discoloration may have an arsenical origin, for in both diseases arsenic is often administered for long periods of time.

What are the minute changes in the pigmented skin? Our patient, grateful that the cause of his trouble had been discovered, volunteered to give us a bit of tissue for microscopical study. Accordingly, a small piece of skin was excised from the lumbar region.

In this specimen the epidermal cells are not hyperpigmented; the corium is the seat of the discoloration. The pigment is distributed almost exclusively about the blood-vessels. Hence, it is seen in the papillæ, but it is most abundant about the basilar layer of capillaries from which the papillary vessels arise. It presents itself in the adventitia of the vascular wall as little brown granules, which lie heaped up to form fine lines, or more frequently very dark ovoid and spindle-shaped groups of about the size of a connective-tissue cell. In many of these collections of pigment nuclei are visible, so that their cellular character is undoubted. The nature of the pigment granule itself is quite obscure. Mr. Hitzrot has kindly made some microchemical tests in the present case, with the same negative results that other observers report. The pigment failed to turn blue when treated with hydrochloric acid and potassium ferrocyanide, and remained unchanged on the addition of ammonium sulphid, or of a five per cent solution of neutral hæmatoxylin. There does not exist the analogy between arsenical pigmentation and argyria that Devergie claimed, for from these experiments it is clear that the pigment contains neither arsenic nor iron. Perhaps, as Geyer suggests, it is hæmatoidin. It is a fact that the long-continued use of arsenic is attended in some individuals by a decided decrease in the hæmoglobin and red blood-corpuscles. The metal itself in chronic poisoning is deposited not only in the liver and spleen, but also in the marrow of the bones; therefore, at the very fountainhead of blood-formation. These observations, added to the microscopical picture, the perivascular deposition, leave little doubt that it is from the disintegration of the blood that the pigment results, but the intimate mechanism of its formation and deposition is entirely unknown.

As to the treatment of arsenical pigmentation, the essential indication is clear. Withdrawal of the drug is usually followed in the course of months by a disappearance of the discoloration. In a few cases the pigmentation has been permanent.

Although melanoderma is a late lesion of arsenical intoxication, keratosis is a still later manifestation, and, in point of time, stands last in the series of arsenical skin eruptions. It is only within the last few years that its arsenical origin has been established beyond dispute. I say beyond dispute in face of the statements made less than two years ago by such eminent dermatologists as Kaposi and Neumann, to the effect that they had never demonstrated with certainty a single case of arsenical keratosis.* After examining this patient and reviewing with me the literature, I will leave you to judge if these statements are warranted by the facts!

Many years ago Romberg wrote of a palmar and plantar affection in association with the use of arsenic. He stated that he had seen exfoliation of the skin in these regions in individuals who had taken the drug.* But, probably the first definite allusion to an undoubted case of arsenical keratosis is made by Erasmus Wilson, in 1868. In discussing the effect of fifteen months' use of the drug on his patient, he writes: "But the most striking evil resulting from the action of the arsenic next to the melasma is the state of chronic erythema of the palmar and plantar surfaces of the hands and feet. These surfaces are red, hot and swollen; the cuticle is dry, harsh, desquamating and covered with hard, dry points, corresponding with the apertures of the sweat-glands, which resemble minute corns, and which she designates by that name."†

In a report of the terrible epidemic at Hyeres, in France, in 1887, where more than four hundred people were poisoned by wine containing arsenic, mention is made of a case in which the epidermis of the soles, particularly about the heels and balls of the toes, became hard and dry and horny.‡ In the same year, at a meeting of some branches of the British Medical Association, held at Gloucester, Mr. Jonathan Hutchinson called attention to several cases of keratoses of the palms and soles, due, he thought, to the ingestion of arsenic. He thought it probable, too, that the drug might cause a peculiar form of cancer.§

The whole subject received important contributions in 1891 by the publication and discussion of three English observations on palmar and plantar keratoses.‖ The third of this series was reported by Pringle as one of "Keratosis of the palms and soles probably of arsenical origin." The patient was a young woman, suffering from psoriasis, who took Fowler's solution for one year. It was then noted that the epidermis of the palms and soles was thickened and keratotic in patches, varying in size from that of a pin's head to that of a pea, so that the skin presented a warty appearance. The affection extended along the lateral borders of the fingers. The description tallies in the main with the case before us. Pringle presented his patient before the Dermatological Society of London, where Mr. Hutchinson gave it as his opinion that the case was one of arsenical keratosis. Considering all of this evidence, there can be at present no doubt as to the existence of such a condition.

The lesion appears after some months or years of arsenical medication, either as a diffuse hypertrophy of the epidermis, or there arise local thickenings of all sizes, giving to the skin a warty appearance. Most frequently, perhaps, the two conditions are combined. Rarely is there any erythema, a circumstance which distinguishes it from the hereditary palmar and plantar keratoses. The palms and soles are usually involved, though, as in this patient, the dorsal and lateral aspects of the fingers and elbows may be affected. As it appears on the

* Ann. de Derm. et de Syph., 1898, t. IX, p. 481.

* Klin. Wahrnehmungen u. Beobachtungen, Berlin, 1851, S. 228.

† Jour. of Cut. Med., 1868, Vol. I, p. 355.

‡ Barthelemy: quoted by Rasch, op. cit., p. 153.

§ An address on the study of skin diseases as illustrating the doctrines of general pathology. Brit. Med. Jour., 1887, II, p. 230.

‖ Brooke: Brit. Jour. of Dermat., 1891, p. 19. Crocker: *ibid.*, p. 169. Pringle: *ibid.*, p. 390.

elbows it recalls the condition of psoriasis, hence Mr. Hutchinson's term "arsenical psoriasis."

By what mechanism the lesion is produced is far from clear. Excessive sweating of the palms and soles has been observed during the long-continued administration of arsenic. It may be that, owing to this hyperhidrosis, arsenic is excreted in the sweat in an unusual amount and that the prolonged contact of the drug in these regions may determine the localization of the lesion. The appearance of the "corns" about the apertures of the sweat-glands has been noted in a few instances.

When the arsenic is withdrawn the keratosis usually remains stationary or slowly diminishes. Active treatment with such preparations as salicylic acid should not be undertaken without bearing in mind a third and less fortunate termination of these keratoses, to which Mr. Hutchinson* drew attention at a meeting of the Pathological Society of London, in 1887. Here he elaborated the proposition which he had made at Gloucester that the internal administration of arsenic could be the cause of a "peculiar form of cancer." He presented notes and drawings of three cases in which, following the use of arsenic, not only palmar and plantar keratosis developed but also malignant growths. His thesis drew forth some opposition, but Sir James Paget, who occupied the chair, remarked that he "had seldom heard an argument founded on clinical and pathological evidence more definitely suggesting the conclusion advanced." Mr. Hutchinson's first case was that of a man suffering from psoriasis who had taken arsenic for many years. "Corns" developed on his hands and feet. A corn on the sole of the foot ulcerated, resembling at first a perforating ulcer. According to Sir James Paget's opinion, "the disease was cancerous." Microscopical examination was inconclusive. The growth was removed; the patient recovered.

The second case was one of unusual interest. An American physician had taken arsenic for psoriasis for a long period. The psoriasis was cured, but the skin of the palms and soles became rough. Fungous ulcerations appeared on both hands. Ultimately both hands were amputated. Eighteen months later the patient died. Metastases of epithelioma were found in the left axillary glands, in both lungs, in the suprarenal glands, and in a rib. I shall refer to this case later on.

Finally, the case of a clerk, aged 34 years, who had taken arsenic for a long time for psoriasis, was cited. When he appeared at the Skin Hospital the palms and soles were dotted with "corns." Then an epithelioma of the scrotum appeared. It was excised, but the subsequent movements of the patient could not be followed.

Now, the facts which were thus brought forward were not unknown, but Mr. Hutchinson's interpretation was novel. Thus, in 1874, an epithelioma taken from the foot of an individual suffering from psoriasis is exhibited before the Anatomical Society of Paris.† A few years later, Cartaz‡ reports to the same society the case of a man forty years of age, suffering from psoriasis, in whom a cancerous ulceration developed over the palmar surface of the right ring finger.

Both patients showed keratoses. They had presumably been treated with arsenic as is practically every case of psoriasis though no mention is made of this fact.

In 1885, Dr. J. C. White,* published an article with the title: "Psoriasis, Verruca, Epithelioma, a sequence." Two cases are reported. The first patient was a man who had had psoriasis of many years' standing. He had taken arsenic in considerable doses. For ten years he had had keratoses on his hands. Three years previous to his examination by Dr. White in 1884 one of these "warts" on the anterior aspect of the right palm ulcerated and a similar but less extensive change took place on the left palm between the fore and middle fingers. The ulcers were viewed as epitheliomata, but before resorting to a radical operation, the patient sought the advice of Mr. Hutchinson and others in Europe. Mr. Hutchinson has pictured the patient's hands in his Archives of Surgery.† To his opinion and the subsequent history of the patient I have already alluded in referring to his second case. Let it be added that microscopically the growths proved to be epitheliomata. Dr. White at the same time reported the case of another man, 52 years of age with psoriasis of long standing, warts on the hands and an epitheliomatous ulcer on the anterior aspect of the right wrist and palm. He, too, had been subjected to an arsenical treatment. White considered the psoriasis as a cause of carcinoma through an intermediate lesion, the wart. At that time arsenical keratosis was not recognized. Even now in hearing the reports of these cases of "arsenical cancer," to use Mr. Hutchinson's term, the fact that all the patients were subjects of psoriasis must draw the critic's attention. It may be true that psoriasis with its hyperplasia of the epidermis predisposes to the formation of epithelioma in individuals submitted to continued arsenical medication, but that it is not a necessary condition is illustrated by a case of Ullman,‡ presented to a society of physicians in Vienna in 1898. The patient, a young woman, had been taking Fowler's solution seven or eight years for a facial acne. A palmar and plantar keratosis followed. During the preceding year an epithelioma appeared on the face. It was extirpated. Six months later, another epithelioma which had developed on the thickened skin of the heel, was removed. Here the cutaneous disease, the acne, can have played no rôle, not even that of a predisposing factor, in the development of the new growth. Still more conclusive are the reports of the cases from Reichenstein.§ The three individuals whose histories, Geyer gives had all been saturated with the arsenical drinking water; had acquired the "Reichenstein complexion," and keratosis of the hands and feet. Each suffered from an epithelioma of the right hand.

In a majority of the cases I have now reviewed, the cancer has appeared either on the hands or feet, regions peculiarly susceptible to arsenical keratosis. Indeed, where the details have been carefully observed, it has been noted that the

* Brit. Med. Jour., 1887, II, p. 1280.
† Pozzi, Bullet. de la Soc. Anat., 1874, p. 587.
‡ Bullet. de la Soc. Anat., 1877, p. 549.

* Am. Jour. of Med. Sc., 1885, Vol. LXXXIX, p. 163.
† 1891, Vol. II, plate XX.
‡ Ann. de Derm. et de Syph., 1898, t. IX, p. 481.
§ Op. cit.

FIG. 1.—Shows the diffusely thickened skin of the palm, the deepening of the cutaneous furrows and the scattered keratosis.

FIG. 2.—Shows the horny excrescences on the sole of the foot. Their distribution suggests the pressure of the shoe as a determining factor in their localization.

epithelioma most often arises directly from these keratotic patches.

This fact is not remarkable, knowing how frequently the keratoses of old age undergo a similar change. Nor is it surprising that the "arsenical warts" of the right hand, constantly exposed to trauma and irritation, most often suffer these changes.

In one of Mr. Hutchinson's cases, the scrotum was the seat of the epithelioma. This localization is of interest in view of the fact that it is an old observation, that the external genitalia are points of predilection of arsenical lesions. Dr. Paris writing in 1825 concerning the poisonous effects of arsenious acid on plants and animals states that "the smelters are occasionally affected with a cancerous disease of the scrotum similar to that which infects the chimney-sweeps."* You see that the very localization of the epitheliomata in these cases favors Mr. Hutchinson's proposition that arsenic "may be the cause of cancer."

To sum up: The present case has given us an opportunity to review a number of interesting and important facts in connection with the administration of arsenic. We have seen that its prolonged use is at times attended with wide-spread pigmentation or keratosis chiefly palmar and plantar, or both pigmentation and keratosis. Associated together, they form a picture which can scarcely be mistaken. The keratosis may in rare instances undergo epitheliomatous changes and lead to a fatal termination. The possibility of such a serious outcome, let alone other accidents of arsenical intoxication, emphasizes once more that arsenic is no indifferent drug. The occurrence of these dermatoses, however, is not to be viewed as the result of a medical error in its administration. Its use continued for months, and at intervals even for years, is the only relief on which many sufferers from psoriasis can rely.

As with other drugs the range of individual susceptibility is wide. While one will develop a keratosis after a few months of arsenical medication, another may take the drug for years with impunity. Mr. Hutchinson has recorded a life-long use of arsenic for the relief of psoriasis in a man sixty years old.* Speaking generally, it had not interfered with his health.

Strange to say, too, I can find no record of these cutaneous accidents we have been considering among the Styrian arsenic-eaters. That arsenic may be habitually used without deleterious effects, and tolerance to large doses established, is illustrated by Mr. Hutchinson's case and the experience of the Styrian peasants, but such an immunity in medical practice is not the rule. Even Mr. Hutchinson's patient suffered from passing, but nevertheless profound, disturbances which might very well be attributed to the drug. From all of which I conclude that without a definite indication prolonged treatment with arsenic is an error.

A common acne may be combated by simpler and less serious measures than years of arsenical medication! On the other hand, as I have just said, for certain cases of psoriasis and let me add, of lichen ruber, chorea, some grave anæmias, and occasionally for retarding the growth of various malignant tumors, the prolonged use of arsenic is a veritable boon. But in these instances its administration must be under medical supervision and not determined, as in the case of the patient before you, by his fears and opinions. "Virtue itself turns vice, being misapplied."

*Quoted in Butlin's Lectures on Cancer of the Scrotum. Brit. Med. Jour., 1892, Vol. II, p. 67. See also, Brouardel, Troubles de l'appareil cutané dans l'arsenicisme. Gaz. hebd. de Med. et de Chir., 27 juin, 1897, p. 603.

*Arch. of Surgery, 1892, Vol. IV, p. 104.

UNCONTAMINATED URINE.

By Howard A. Kelly, M. D., *Gynecologist-in-Chief, The Johns Hopkins Hospital.*

THE BEST WAY TO SECURE UNCONTAMINATED URINE FROM THE BLADDER AND FROM THE KIDNEY, AND HOW TO MINIMIZE THE RISKS OF CATHETERIZATION IN WOMEN.

The question of catheterization is ever a burning one, whether in the large clinic after important pelvic operations, where it is conducted on a wholesale scale, or in the case of the single patient at her home after confinement. In view of the frequent immediate untoward results of catheterization and their distressing sequelæ, I think we might almost reckon this procedure among the major gynecological operations, until the question as to the safest method is finally solved.

The first query of importance is, "Who shall catheterize the patient—shall the doctor or the nurse?" A little consideration will show that it would be practically impossible for the doctor, often at a distance and otherwise engaged, to add this to his already burdensome duties, and it must therefore be looked upon as distinctively a nurse's duty. (See Fig. 1.)

To this end the nurse must be especially trained; she must be warned of the unusual risks and taught each step with great exactitude. The method I have adopted for some years past in my own clinics is the following:

I prefer to use a glass catheter, which I first tried in 1884, when I made one extemporaneously for an urgent case out of the glass tube of a baby's feeding-bottle; the glass is easily kept clean, and can be introduced *without touching the end which enters the bladder.* (See *Amer. Jour. Obs.*, February, 1889, p. 184.) (See *Kuestner Centralb. f. Gyn.*, 1890, No. 23.) (See also an excellent article by Prof. Kuestner, on glass catheters, as a means of prophylaxis against cystitis in women, *Deutsche med. Woch.*, 16 May, 1883.)

Each patient has her own catheter for her exclusive use as long as she needs one. *It is sterilized by boiling* five minutes in a soda solution and then placed in an open-mouth bottle

filled with 5 per cent carbolic solution, or 1-1000 bichloride of mercury with some cotton on the bottom to protect the end of the catheter.

Just before using it may be boiled again in the soda solution.

The nurse then scrubs her hands carefully and places the patient on a bed-pan and exposes the vulva and separates the labia so as to *expose the urethral orifice.*

She now takes up a pledget of cotton, saturated with a boric-acid solution, in the grasp of a forceps, and with this thoroughly *cleanses the urethral orifice.* This is repeated with another pledget when the patient is ready for catheterization. (See Fig. 2.)

She now draws two *sterile finger-cots* over her thumb and index finger of the right hand, and thus well protected *grasps the catheter by its outer end* and removes it from the receptacle, rinses it off with sterile water, or if it has just been boiled lifts it directly from the pan, and gently introduces it into the urethra, allowing it to take its own way into the bladder and *never under any circumstances using force.*

I desire here to point out the fact that *the catheter never completely empties the bladder when the patient is lying down*; and if there is any cystitis it is best to wash it out, using a large catheter with a strong curve at its vesical end. After the irrigation the curved end is turned downwards towards the base of the bladder, when the sediment often escapes first.

Uncontaminated urine may be obtained from the bladder for bacteriological study in the following manner:

The catheter is sterilized with a piece of rubber tubing covering an inch or more of its outer end and projecting about 2 inches beyond it. It is then introduced, preferably by the physician, with the precautions described, and the urine allowed to escape for a few seconds, after which the rubber sleeve is pulled off and the urine now running over the sterilized end of the catheter is collected in a test-tube. In my investigations of several hundred specimens in this way conducted with my associate, Dr. Thos. R. Brown, we have had no cases of accidental contamination. *In twenty instances sterile urine was taken as a control experiment and in every case it remained sterile.* (Fig. 3.)

In securing uncomtaminated urine from the kidney, I proceed in a similar manner. The bladder is washed out and emptied, and the patient is put in the knee-breast posture and the ureteral orifice exposed. This may now be cleansed with a little pledget of boric-acid solution and the catheter introduced.

The catheter is sterilized with a rubber sleeve protecting and projecting beyond the end. The operator draws on the hand which grasps the catheter a sterilized half-glove, which I have had made for this purpose, and grasping the catheter, protected also if need be by a sterile towel on his shoulder, he introduces the end into the ureter and pushes it on up into the kidney. The patient is then allowed to lie down on her side or on her back, the sleeve is pulled off, and the sterile end of the catheter is put in a sterile test-tube held in place by the cotton plug.

I have done this not less than sixty times and have never yet seen an accidental contamination.

It is evident, therefore, that by this procedure, when the ureter is catheterized by my method through the open speculum in an air-distended bladder, we possess a method of securing cultures from infected kidneys which is impossible in any other way short of a surgical operation.

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ROBERT REULING, M. D. Changes in the Skin in Paralysis Agitans.—*Maryland Medical Journal*, March, 1900.

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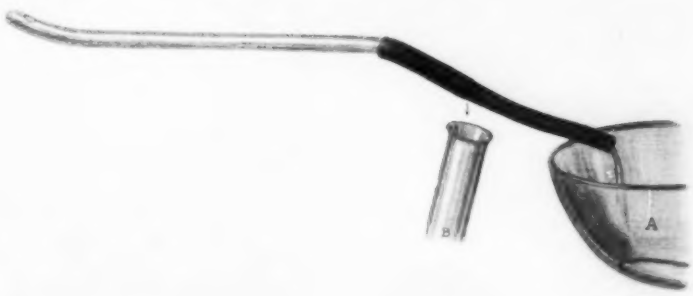


FIG. 1.—The sterilized glass catheter, protected by a rubber sleeve. When first introduced, a little urine is allowed to escape into the vessel A; then the rubber sleeve is pulled off, and uncontaminated urine runs directly from the end of the glass tube into the sterile tube B.

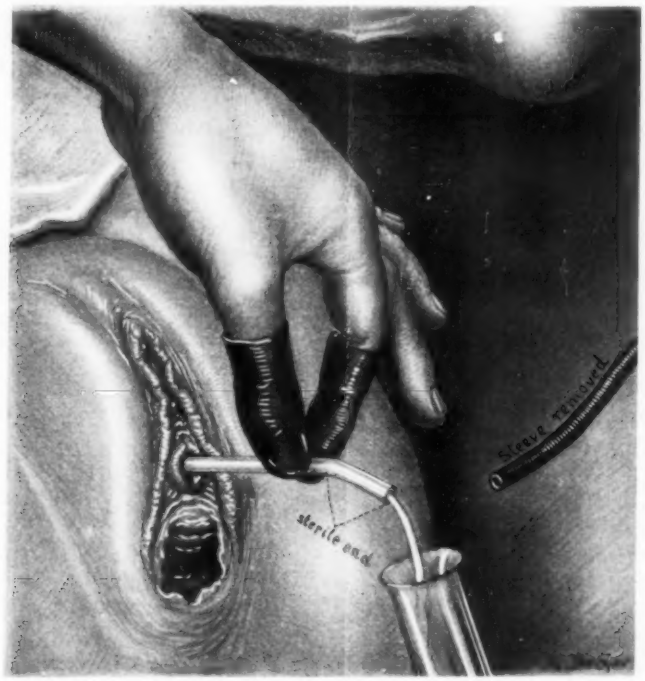


FIG. 2.—Shows the nurse holding the catheter with fingers protected by sterile rubber finger cots, while the urine escapes from the sterile end into the glass tube upon removal of the rubber protecting sleeve.

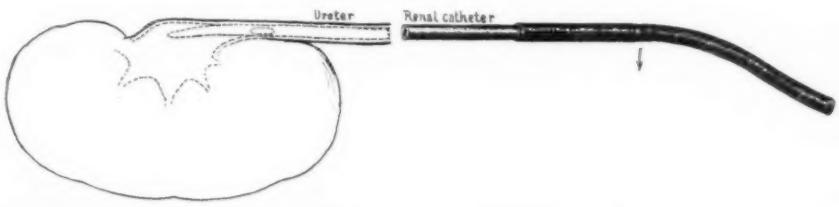
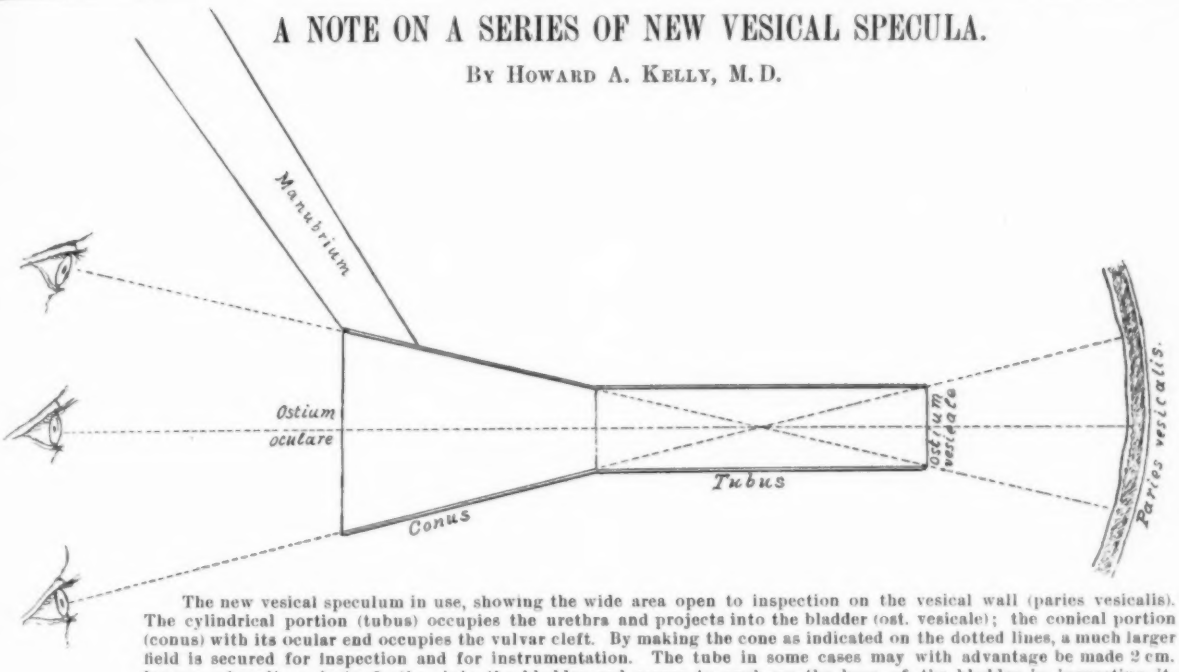


FIG. 3.—The renal catheter protected by the rubber sleeve. On introduction, the sleeve is pulled off and the end of the catheter, marked by the arrow, inserted in a sterile tube and uncontaminated urine collected.

A NOTE ON A SERIES OF NEW VESICAL SPECULA.

By Howard A. Kelly, M. D.



The new vesical speculum in use, showing the wide area open to inspection on the vesical wall (paries vesicalis). The cylindrical portion (tubus) occupies the urethra and projects into the bladder (ost. vesicale); the conical portion (conus) with its ocular end occupies the vulvar cleft. By making the cone as indicated on the dotted lines, a much larger field is secured for inspection and for instrumentation. The tube in some cases may with advantage be made 2 cm. longer, when it projects further into the bladder and serves to push up the base of the bladder in inspecting it.

The open cylindrical vesical speculum when in use is topographically divided into a urethral and a vulvar portion.

The calibre of the urethral portion is limited by the degree of safe or convenient distention of the urethra, and in the average specula ranges from No. 9 to No. 12 (the numbers in my scale representing millimetres in diameter); in the larger sizes, used for operations, the calibre may even be carried as high as 20 mm., the limit of a safe degree of dilatation, as shown by Simon.

The vulvar portion, however, has no such necessary limitations and may, as I have found, be expanded with great advantage into a broad funnel. The best form of funnel is one in which the angles formed by the lines of the slanting sides meet exactly in the middle of the tubular portion. This gives a maximum area of inspection and a maximum room for treatment, especially in using instruments with crossed blades. The length of each of these parts of the speculum should be 5 cm.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Monday, February 19, 1900.

The Pathological Findings in a Case of General Cutaneous and Sensory Anæsthesia.—Dr. Berkley. (See Bulletin for March.)

Specimens of False Porencephalia. Dr. Berkley.—The person from whom this specimen was obtained was a medium-grade imbecile, who had lived to reach the age of 58 years. He was tall, with fairly developed musculature, and without marked cranial deformity. At the autopsy, the brain weighed 950 grammes. The convolutions on the external aspect of the hemispheres were without any marked asymmetries, but the right half of the brain was considerably smaller than the left, and when taken out of the bony envelope, flattened perceptibly. On closer examination, a defect was found on the median-inferior aspect of the hemisphere, measuring four centimetres in its greatest length by two in its greatest width. The anterior margin lay considerably forward of the splenium of the corpus callosum, the posterior end stopped three and a half cm. before the tip of the occipital lobe. The defect was separated from the ventricle by a leathery substance, from 1.50 to 1.75 mm. in thickness. This showed no trace of cerebral matter. The lesion formed a pocket beneath the general level of the surrounding brain-tissue, which was filled with a gelatinous mass. The convolutions involved were portions of the posterior end of the convolution of the corpus callosum, the anterior and middle parts of the lingual convolution, the innermost aspect of the occipito-temporal gyrus, and a large part of the convolution of the hippocampus. The cuneus was not disturbed. The foot of the hippocampus was not entirely destroyed, its anterior portion retaining some of the nerve elements. In the posterior portion of the hippocampus the traces of an old hemorrhage were found, showing that the lesion had originated in the rupture of a blood-vessel. The corpus callosum throughout its whole extent was poorly developed, but the posterior half was especially thin, an evi-

dence that the injury to the cortex had taken place in early life, and that the hemispheres had not fully developed thereafter. When the right and left sides of the corpus callosum were compared in the cross-sections, the left side was seen to be thinner than the right. There were no indications of localized brain lesion during life.

On a Form of Conjugation of the Malarial Parasite.—Dr. Ewing.

In four cases of tertian infection the writer has encountered appearances in the blood which seem to admit of no other explanation than that of conjugation of malarial parasites. In a considerable number of other cases similar appearances were found, but much less frequently.

The blood in these cases showed a large number of young rings and many half-grown and full-grown forms. A great many cells showed double infection with young rings. In many instances these rings were entirely separate, each exhibiting a single large granule of chromatin. Many cells, however, contained two rings, which were clearly fused together along one segment of the ring, and two large chromatin granules were then invariably found at different points in the rings. The fused parasites usually differed in appearance. One was a large delicate ring with a thin bow, and chromatin granule of moderate size, while the other was a coarser body with thickened bow, enclosing little or no hæmoglobin, and exhibiting a large chromatin granule.

Among the single rings, these two forms of young parasites were often distinguished, but no single rings could be found containing two equally large chromatin granules, while every red cell that exhibited two large and equal chromatin granules contained also two distinct rings. It appears, therefore, that the bodies of many parasites had become fused together, while their nuclei remained separate.

On examining the parasites in later stages of development, most of them were found to have lost the ring form and to have spread out into a large number of threads, with nodal thickenings variously curled in the red cell. These threads evidently represented the pseudopodia of a very active amœboid stage. The chromatin masses were now subdivided into ten or twelve granules; but, in the majority of the cases, these masses were far apart and showed no tendency to unite. In many cells, however, the amœboid figures were less marked, and the masses of chromatin lay side by side, united by a little achromatic substance. Later some parasites were found in which the two groups of rather large chromatin granules lay in immediate apposition, surrounded by achromatic substance. This phase was marked by a distinct reduction in the length of amœboid figures.

Many older spheroidal, hyaline forms, belonging to this same brood, were found in these cases, but all the older hyaline forms were single, and exhibited a single large group of fine chromatin granules. Not one cell harboring two full-grown parasites could be found in prolonged and repeated searches through several slides. Whatever interpretation may be placed upon this peculiar absence of older twinned forms, the finding of all stages of union, first of the bodies and later of the nuclei, likewise appears to admit of no other explanation than that of conjugation.

Dr. Welch.—I have been greatly interested in Dr. Ewing's paper, and consider that the Society is to be congratulated upon this opportunity to listen to his personal presentation of these important observations. There can be no question as to the accuracy of these observations, whatever difference of opinion there may be in their interpretation. Most of the questions which had occurred to me in the course of Dr. Ewing's remarks, he answered before their conclusion.

The most important question seems to me whether the conjugation of parasites described by Dr. Ewing, is to be looked upon as something essential, really pertaining to the life history of the organism, or as merely a more or less accidental coalescence, or fusion, of two cells. Of such fusion of cells we have some examples in normal and pathological processes, and if this latter be the proper interpretation, there may be some question as to the propriety of the designation "conjugation," which has a special meaning among biologists. I do not know that Dr. Ewing is in a position to express himself more definitely upon this point.

Dr. Thayer.—We all, I am sure, feel grateful to Dr. Ewing for the very interesting communication which he has made. I regret extremely that Dr. Lazear is not here to take part in the discussion, inasmuch as he has for the past year been making careful studies in this line. Unfortunately, he has gone to Cuba, and his specimens and the paper which I had expected to have in time to read to-night have not been received.

Dr. Ewing's interpretation of his interesting observations is extremely suggestive. I recognize many of the pictures which have been described, but I must confess that their possible importance had escaped me. I have, without much thought, always assumed that the reason why twin parasites were relatively common in the early stages of development of the organism and so infrequent later on was that with the growth of the several contained organisms the red blood-corpuscle was eventually ruptured, both parasites escaping and meeting the fate which apparently inevitably befalls extracellular bodies at this stage of development. But, after all, this is a pure hypothesis, and in view of Dr. Ewing's careful studies I should surely feel called upon to thoroughly restudy the question before venturing to dispute his conclusions.

A rather interesting point in connection with this matter, if we are to regard the process as one of fusion, is that at a certain stage the structure of the organism might justify the term *plasmodium*, the biological inaccuracy of which as applied to the ordinary parasites has been so generally recognized.

In connection with the possibility that this process might be a true conjugation, a rather inviting, though I fear improbable, explanation of its possible significance suggested itself to my mind.

In the æstivo-autumnal parasite, for instance, beside the organisms pursuing the ordinary cycle of development, there soon appear other bodies morphologically distinct from these, the crescentic and ovoid forms. These forms, Mannaberg

contends, are the result of conjugation of two elements belonging to the ordinary cycle.

Only from the bodies belonging to the crescentic group do the sex-ripe forms (macrogametes and microgametocytes) develop.

In a recent communication Bastianelli and Bignami assert that the sex-ripe forms in the tertian parasite likewise develop from elements morphologically distinguishable from those belonging to the ordinary cycle.

What causes the differentiation of the crescent group in the æstivo-autumnal parasite and of the group destined to develop into sex-ripe forms in the tertian parasite? May it be that these sex-ripe forms in both instances develop only as a result of conjugation of two bodies, each of which alone would be capable of pursuing only the ordinary asexual cycle—that the process observed by Dr. Ewing is a necessary stage in the production of elements destined to develop into flagellate forms (microgametocytes) or macrogametes?

I am, however, unaware whether there is any analogy to justify such an hypothesis—and what is more important the fact that the crescents are formed as a result of conjugation is by no means settled. Indeed, we are inclined to believe, with the Italians, that this is not the case.

Dr. MacCallum.—I would like to ask one or two questions of Dr. Ewing. 1st, Whether he has seen any actual fusion of the chromatin bodies, or whether they simply lie side by side as he has pictured them; and, 2d, What happens after this—whether there is any difference between the conjugated forms and the others. As I understood him, they both go on to sporulation; and it struck me as an occurrence which has its parallel in certain lower animals, that conjugation should take place in these young immature cells. I would also like to know whether he has observed this only in one cycle or in several successive cycles.

Dr. Ewing.—When I made up my mind to read this paper in Baltimore, it was with the idea that I could obtain more information here than anywhere else on a point which concerns the minute morphology of the malarial parasite. This decision seems to have been justified, and I feel that I am now in a better position to consider the importance of this process.

Dr. Welch has hit the nail on the head in regard to the significance of the process. I am fully convinced that all the stages I have described actually occur, but it is a totally different thing to ascribe to such a process its proper interpretation. I am inclined to think that this process has not the full significance we find it to have in certain lower animals where conjugation is a *necessary* preliminary to sporulation. It is certainly not so of the malarial organism. I only claim that it occurs frequently, and is a real fusion of parasites, undergone for convenience, perhaps, but is not an essential preliminary to sporulation. I thank Dr. Welch very much for making the suggestion that clearly places the process in its correct position.

I confess that I had not had in mind the possibility that when two parasites conjugate the result might be the rupture of the cell and death of both parasites. I had suspected that some one might claim that one parasite, gaining the upper-hand, had destroyed the other, but it had not entered my mind that both might be thrown out.

Now, what can be said as to the possibility of such a process occurring? It seems to me that if it does occur with any frequency, it would occasionally be observed in some specimen; and it seems, on general principles, extremely unlikely that if such a rupture and extrusion occurs, we should examine hundreds of specimens and fail to find any trace of such a process. I have been over these slides until my eyes hurt, and have not found any traces of the rupture of cells and extrusion of twin parasites. The suggestion is an extremely good one, however, and I shall hereafter bear it mind. I am somewhat surprised that I did not think of it before, and I want to thank Dr. Thayer for the suggestion.

In regard to Dr. Thayer's suggestion concerning the relation of this process of conjugation to the life history of the parasite and preparing it for growth in the musquito, I have not allowed myself to draw any conclusions whatever on that point. I am inclined to think, with Dr. Welch, that it is a mere fusion taking place when they are very numerous, and has probably nothing to do with the development of flagellate bodies or of any form especially adapted to growth in their new host. It seems rather to increase the numbers of young parasites produced in the human host. I was unable to trace the full development of some of the single parasites. This, also, is an extremely important point, and is the one I had foremost in mind in discussing the subject. I have noticed in these conjugating specimens that I can hardly ever get any flagellate bodies.

Dr. MacCallum wishes to know if I have actually seen fusion of the nuclei. I have not. I do not see how it is possible in the fresh specimen to accurately follow the process of union of masses of chromatin, such as we are dealing with here. My experience is that only the grosser processes can be identified with certainty by such means, and I feel that the identification of the nuclear bodies in the fresh specimen, as concerned in this process, would be unreliable in my hands. I should prefer to leave that to some one more familiar with the study of fresh-blood specimens. I do believe very firmly, however, that such union of nuclei does occur, from study of stained specimens. The same answer applies to his last question: Have I followed the development through several generations or only in one? I have not been able to follow up more than one generation, because we are in New York seldom able to follow these cases long. In the cases of the soldiers at Montauk, I had to take many specimens within a few minutes and usually saw the patient but once.

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